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Atrial fibrillation, cognitive impairment, and neuroimaging

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Abstract

Introduction: The objective of our study was to investigate cross-sectional associations of atrial fibrillation with neuroimaging measures of cerebrovascular disease and Alzheimer's disease and their interactions with mild cognitive impairment (MCI).

Methods: Magnetic resonance imaging scans of individuals from a population-based study were analyzed for infarctions, total gray matter, and hippocampal and white matter hyperintensity volumes. A subsample underwent positron emission tomography imaging.

Results: Atrial fibrillation was associated with infarctions and lower total gray matter volume. Compared with subjects with no atrial fibrillation and no infarction, the odds ratio (95% confidence intervals) for MCI was 2.99 (1.57–5.70; $P = .001$) among participants with atrial fibrillation and infarction, 0.90 (0.45–1.80; $P = .77$) for atrial fibrillation and no infarction, and 1.50 (0.96–2.34; $P = .08$) for no atrial fibrillation and any infarction.

Discussion: Participants with both atrial fibrillation and infarction are more likely to have MCI than participants with either infarction or atrial fibrillation alone.

Keywords: Atrial fibrillation; Mild cognitive impairment; Stroke; Alzheimer's disease; Cerebrovascular disease

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1. Introduction

The lifetime prevalence of atrial fibrillation among individuals aged ≥40 years is approximately 25% [1]. The prevalence of dementia among those >71 years is approximately 13.9% [2]; (10% in Mayo Clinic Study of Aging [MCSA] [3]. Both atrial fibrillation and dementia increase with age. Numerous studies have reported an association between atrial fibrillation and dementia [4,5] or cognitive impairment [6–8]. The association remains after controlling for both a history of clinical stroke [8–10] and shared risk factors of atrial fibrillation and dementia. A number of mechanisms have been postulated for this independent association including cerebral hypoperfusion [11,12], silent infarction [5], and even Alzheimer's disease (AD) [13]. Similar to prior studies, the MCSA reported that atrial fibrillation was associated with mild cognitive impairment (MCI), specifically nonamnestic MCI [14]. The objective of this study was to investigate the cross-sectional associations of atrial fibrillation with multimodality neuroimaging measures of cerebrovascular disease and AD-related pathology and their interactions with regard to MCI.

2. Methods

2.1. Study participants

Participants were enrolled in the MCSA, a longitudinal population-based study designed to investigate predictors of MCI and dementia. The study design of the MCSA has been published previously [15]. Briefly, at the study onset, Olmsted County residents aged 70–89 years were identified using the Rochester Epidemiology Project medical records–linkage system. An age- and sex-stratified sampling strategy was used to randomly select nondemented subjects for participation in the study. In 2005, participants were invited to undergo magnetic resonance imaging (MRI) imaging. In 2006, participants were invited to undergo positron emission tomography (PET) imaging.

2.2. Cognitive evaluation

Participants were evaluated at baseline and every 15 months by a study coordinator, physician, and neuropsychometrist. The neuropsychometrist administered nine tests covering four domains including memory, executive function, language, and visuospatial skills. The diagnosis of MCI was based on published criteria [16]. The diagnosis of MCI was made by a consensus decision by the behavioral neurologist, neuropsychologists, and study coordinator who saw the participant after consideration of education level, occupation, and sensory impairment (hearing or vision) [3,15].

2.3. Clinical data acquisition

Clinical data including history of hypertension, smoking, diabetes, dyslipidemia, history of stroke, and coronary artery disease factors were obtained by nurse abstraction of information from the detailed medical records included in the medical records–linkage system [17]. Silent infarction was defined as no history of clinical stroke in the medical record or Hachinski score but the presence of stroke on neuroimaging.

2.4. Criteria for atrial fibrillation

Criteria for atrial fibrillation were based on a physician diagnosis, electrocardiographic evidence of atrial fibrillation, and/or treatment for atrial fibrillation using the medical records–linkage system from the Rochester Epidemiology Project. Using this method, patients with postoperative atrial fibrillation were included. These data were abstracted by trained research nurses.

2.5. MRI acquisition

FLAIR-MRI and MPRAGE images were acquired with 3T MRI scanners, and the complete details of the acquisitions can be found elsewhere [18]. The MPRAGE (structural MRI) images were used to obtain the total gray matter volume estimates and hippocampal volumes using Freesurfer (version 5.3) [19], and the hippocampal volume was adjusted for total intracranial volume (TIV) as previously described [20]. The FLAIR-MRI was used to ascertain three components of vascular disease—subcortical infarcts, cortical infarcts, and white matter hyperintensities (WMHs). All the brain infarcts were assessed by a trained image analyst and confirmed by a radiologist (K.K.) blinded to all clinical information. Subcortical infarcts included infarcts in white matter (WM), deep gray matter nuclei, cerebellum, and brain stem not involving the hemispheric infarcts. Cortical infarcts were ≥1 cm in largest diameter. Intrarater reliability of this assessment is excellent (proportion in agreement 0.98 for cortical and 0.94 for subcortical infarcts) [21]. WMHs on FLAIR images were segmented using an automated slice-based seed initialization and region growing methods as previously described [22]. We used WMH divided by the TIV as a measure of WM disease.

2.6. 18F-FDG PET and 11C-PiB PET acquisition

PET images were acquired with a PET/computed tomography (CT) operating in three-dimensional mode (septa removed). The complete details of PET acquisition were described previously [23,24]. The global cortical PiB PET retention ratio was calculated by averaging the PiB retention ratio from AD signature regions normalized to cerebellar uptake [25]. Similarly, an AD signature ^{18}F-FDG PET ratio was calculated for brain glucose metabolism from an AD signature meta-ROI with normalization to pons glucose uptake [26–28]. We performed the analysis with and without partial volume correction.